IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

EURAND, INC.
845 Center Drive
Vandalia, Ohio 45377

Plaintiff,

v.

HON. JON W. DUDAS,
Under Secretary of Commerce for
Intellectual Property and Director of the
United States Patent and Trademark Office,
Office of General Counsel, United States
Patent and Trademark Office, P.O. Box
15667, Arlington, VA 22215
Madison Building East, Rm 10B20, 600
Dulany Street, Alexandria, VA 22314

Defendant.

Case: 1:08-cv-02170
Assigned To : Collyer, Rosemary M.
Assign. Date : 12/12/2008
Description: Admin. Agency Review

Plaintiff Eurand, Inc. ("Eurand"), for its complaint against the Honorable Jon W. Dudas, states as follows:

NATURE OF THE ACTION

1. This is an action by the assignee of United States Patent No. 7,387,793 ("the '793 patent") seeking judgment, pursuant to 35 U.S.C. § 154(b)(4)(A), that the patent term adjustment for the '793 patent be changed from 470 days to at least 655 days.

2. This action arises under 35 U.S.C. § 154 and the Administrative Procedure Act, 5 U.S.C. §§ 701-706.

THE PARTIES

3. Plaintiff, Eurand is a corporation, organized, existing and doing business under and by virtue of the laws of the State of Nevada, with its office and principal place of business located at 845 Center Drive, Vandalia, Ohio, 45377.

4. Defendant Jon W. Dudas is the Under Secretary of Commerce for Intellectual Property and Director of the United States Patent & Trademark Office ("PTO"), acting in his official capacity. The Director is the head of the PTO and is responsible for superintending or performing all duties required by law with respect to the granting and issuing of patents, and is designated by statute as the official responsible for determining the period of patent term adjustment under 35 U.S.C. § 154.

JURISDICTION AND VENUE

5. This Court has jurisdiction over the subject matter of this action and is authorized to issue the relief sought pursuant to 28 U.S.C. §§ 1331, 1338(a) and 1361, 35 U.S.C. § 154(b)(4)(A) and 5 U.S.C. §§ 701-706.

6. Venue is proper in this district by virtue of 35 U.S.C. § 154(b)(4)(A).

7. This Complaint is being timely filed in accordance with 35 U.S.C. § 154(b)(4)(A).

BACKGROUND

8. Plaintiff Eurand is the assignee of all right, title and interest in the '793 patent, as evidenced by records on deposit with the PTO, and is the real party in interest in this case.

9. Gopi Venkatesh and James M. Clevenger are the inventors of the patent application serial number 10/713,929 ("the '929 application").

10. The '929 application was filed on November 14, 2003, and issued as the '793 patent on June 17, 2008, indicating a patent term adjustment of 470 days. The '793 patent is attached hereto as Exhibit A.

11. 35 U.S.C. § 154(b) requires that patent terms be adjusted to compensate for failures of the PTO to take certain actions on patent applications within designated time limits. Specifically, 35 U.S.C. § 154(b)(3)(D) states that "[t]he Director shall proceed to grant the patent after completion of the Director's determination of a patent term adjustment under the procedures established under this subsection, notwithstanding any appeal taken by the applicant of such determination."

12. In calculating the patent term adjustment, the Director must take into account PTO delays under 35 U.S.C. § 154(b)(1), any overlapping periods in the PTO delays under 35 U.S.C. § 154(b)(2)(A), and any applicant delays under 35 U.S.C. § 154(b)(2)(C).

13. Under 35 U.S.C. § 154(b)(4)(A), "[a]n applicant dissatisfied with a determination made by the Director under paragraph (3) shall have remedy by a civil action against the Director filed in the United States District Court for the District of Columbia within 180 days after the grant of the patent. Chapter 7 of title 5 shall apply to such action."

CLAIM FOR RELIEF

14. The allegations of paragraphs 1-13 are incorporated in this claim for relief as if fully set forth herein.

15. The currently challenged patent term adjustment of the '793 patent, as determined by the Defendant under 35 U.S.C. § 154(b), and listed on the face of the '793 patent, is 470 days. (*See* Exhibit A at 1). This determination of the 470-day patent term adjustment is in error. Pursuant to 35 U.S.C. § 154(b)(1)(A), the PTO failed to allow an adjustment for the time exceeding fourteen months after the actual filing date of the '929 application to the date ending on the mailing of an action under 35 U.S.C. § 132. Therefore, the correct patent term adjustment for the '793 patent is at least 655 days.

16. Under 35 U.S.C. § 154(b)(1)(A), Plaintiff is entitled to an adjustment of the term of the '793 patent of 185 days, the number of days attributable to PTO examination delay ("A Delay"). The A Delay consists of the following: A period of 185 days pursuant to 35 U.S.C. § 154(b)(1)(A) due to the PTO's failure to mail an action under 35 U.S.C. § 132 not later than 14 months from the actual filing date of the application. This period consists of the length of time from January 14, 2005 (14 months after the filing date of the '929 application) to July 18, 2005 (the mailing date of the First Office Action).

17. Under 35 U.S.C. § 154(b)(1)(B), Plaintiff is entitled to an additional adjustment of the term of the '793 patent of a period of 581 days, which is the number of days the issue date of the '793 patent exceeds three years from the filing date of the application ("B Delay").

18. Section 35 U.S.C. § 154(b)(2)(A) states that "to the extent . . . periods of delay attributable to grounds specified in paragraph [154(b)(1)] overlap, the period of any adjustment

granted under this subsection shall not exceed the actual number of days the issuance of the patent was delayed." For the '793 patent, none of the A Delay overlaps with the B Delay period. Therefore, these is no period of overlap to be excluded for the patent term adjustment.

19. Thus, the total period of PTO delay is 766 days, which is the sum of the period of A Delay (185 days) and the period of B Delay (581 days).

20. Under 35 U.S.C. § 154(b)(2)(C), the total period of PTO delay is reduced by the period of applicant delay, which is 111 days as determined by the Defendant.

21. Accordingly, the correct patent term adjustment under 35 U.S.C. § 154(b)(1) and (2) is 655 days, which is the difference between the total period of PTO delay (766 days) and the period of applicant delay (111 days).

22. Moreover, Defendant's determination that the period of the patent term adjustment for the '793 patent is only 470 days is in conflict with this Court's decision in *Wyeth v. Dudas*, Civ. Action No. 1:07-cv-01492-JR, 2008 WL 4445642 (D.D.C. Sept. 30, 2008), which explains the proper method for calculating patent term adjustments under 35 U.S.C. § 154(b). The *Wyeth v. Dudas* decision is attached as Exhibit B.

WHEREFORE, Plaintiff respectfully prays that this Court:

A. Issue an Order changing the period of patent term adjustment for the '793 patent from 470 days to 655 days, and requiring Defendant to alter the term of the '793 patent to reflect the 655 day patent term adjustment; and

B. Grant such other and further relief as the nature of the case may admit or require and may be just and equitable.

Respectfully submitted,

Dated: December 12, 2008

By: _____

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Attorneys for Plaintiff Eurand, Inc.

83655 v3/DC

EXHIBIT A

US007387793B2

(12) **United States Patent**
Venkatesh et al.

(10) **Patent No.: US 7,387,793 B2**
(45) **Date of Patent: Jun. 17, 2008**

(54) **MODIFIED RELEASE DOSAGE FORMS OF SKELETAL MUSCLE RELAXANTS**

(75) Inventors: **Gopi Venkatesh**, Vandalia, OH (US); **James M. Clevenger**, Vandalia, OH (US)

(73) Assignee: **Eurand, Inc.**, Vandalia, OH (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 470 days.

(21) Appl. No.: 10/713,929

(22) Filed: Nov. 14, 2003

(65) **Prior Publication Data**

US 2005/0106247 A1 May 19, 2005

(51) **Int. Cl.**
A61K 9/14 (2006.01)

(52) U.S. Cl. 424/489

(58) Field of Classification Search 424/489
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,590,062	A		5/1986	Jang
4,728,513	A		3/1988	Ventouras
4,743,248	A		5/1988	Bartoo et al.
4,780,319	A		10/1988	Zentner et al.
4,789,549	A		12/1988	Khan et al.
4,795,644	A		1/1989	Zentner
4,814,183	A		3/1989	Zentner
4,839,177	A	*	6/1989	Colombo et al. 424/482
4,851,228	A		7/1989	Zentner et al.
4,851,229	A		7/1989	Magruder et al.
4,882,167	A		11/1989	Jang
4,996,047	A		2/1991	Kelleher et al.
5,008,114	A		4/1991	Loverecich
5,120,548	A		6/1992	McClelland et al.
5,260,069	A		11/1993	Chen
5,350,584	A		9/1994	McClelland et al.
5,366,738	A		11/1994	Rork et al.
5,407,686	A	*	4/1995	Patel et al. 424/468
5,422,122	A		6/1995	Powell
5,582,838	A		12/1996	Rork et al.
5,874,418	A		2/1999	Stella et al.
5,882,682	A		3/1999	Rork et al.
5,952,451	A		9/1999	Zhao
6,004,582	A		12/1999	Faour et al.
6,020,000	A		2/2000	Wong et al.
6,451,345	B1		9/2002	Percel et al.
6,500,454	B1		12/2002	Percel et al.
6,627,223	B2		9/2003	Percel et al.
6,663,888	B2		12/2003	Percel et al.
2003/0099711	A1	*	5/2003	Meadows et al. 424/474
2003/0215496	A1	*	11/2003	Patel et al. 424/452
2004/0166160	A1		8/2004	Subramanian et al.
2004/0197407	A1		10/2004	Subramanian et al.

FOREIGN PATENT DOCUMENTS

WO	98/06439		2/1998
WO	98/18610		5/1998
WO	98/53802		12/1998
WO	99/12524		3/1999
WO	WO99/12524	*	3/1999
WO	99/18937		4/1999
WO	99/30671		6/1999
WO	WO99/30671	*	6/1999
WO	01/15668		3/2001
WO	03/020242		3/2003

OTHER PUBLICATIONS

U.S. Appl. No. 10/335,295, filed Dec. 2002, Venkatesh et al.
U.S. Appl. No. 10/619,924, filed Jul. 2003, Venkatesh et al.
Akimoto, M. et al., "Evaluation of sustained-release granules of chlorphenesin carbamate in dogs and humans," *International Journal of Pharmaceutics*, 100, pp. 133-142 (1993).

* cited by examiner

Primary Examiner—MP Woodward
Assistant Examiner—Bethany Barham
(74) *Attorney, Agent, or Firm*—Cooley Godward Kronish LLP

(57) ABSTRACT

A unit dosage form, such as a capsule or the like, for delivering a skeletal muscle relaxant, such as cyclobenzaprine hydrochloride, into the body in an extended or sustained release fashion comprising one or more populations of drug-containing particles (beads, pellets, granules, etc.) is disclosed. At least one bead population exhibits a predesigned sustained release profile. Such a drug delivery system is designed for once-daily oral administration to maintain an adequate plasma concentration—time profile, thereby providing relief of muscle spasm associated with painful musculoskeletal conditions over a 24 hour period.

20 Claims, 4 Drawing Sheets

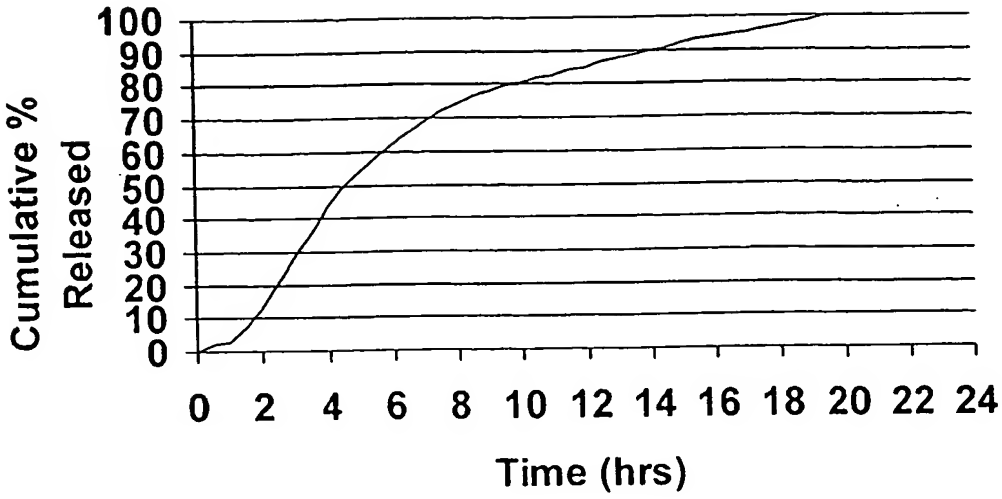
Cumulative % Released
100
90
80
70
60
50
40
30
20
10
0
0 2 4 6 8 10 12 14 16 18 20 22 24
Time (hrs)

FIG. 1

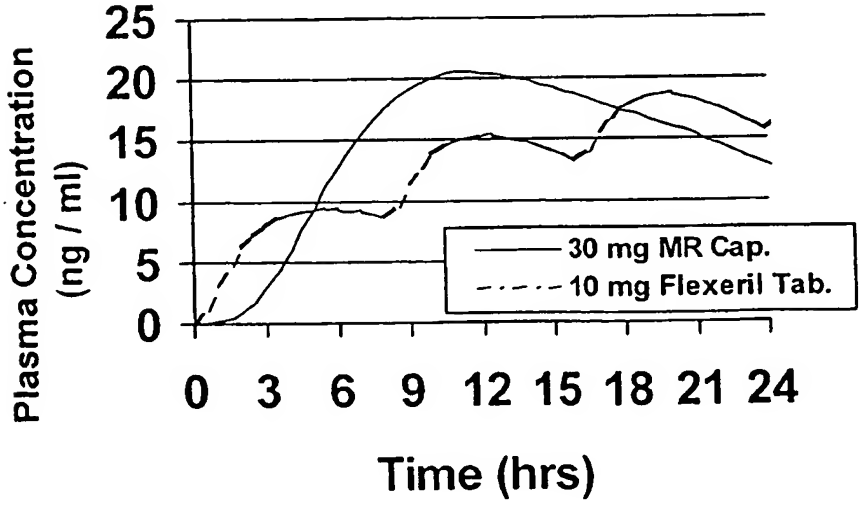
Plasma Concentration (ng / ml)
25
20
15
10
5
0
0 3 6 9 12 15 18 21 24
Time (hrs)
30 mg MR Cap.
10 mg Flexeril Tab.

FIG. 2

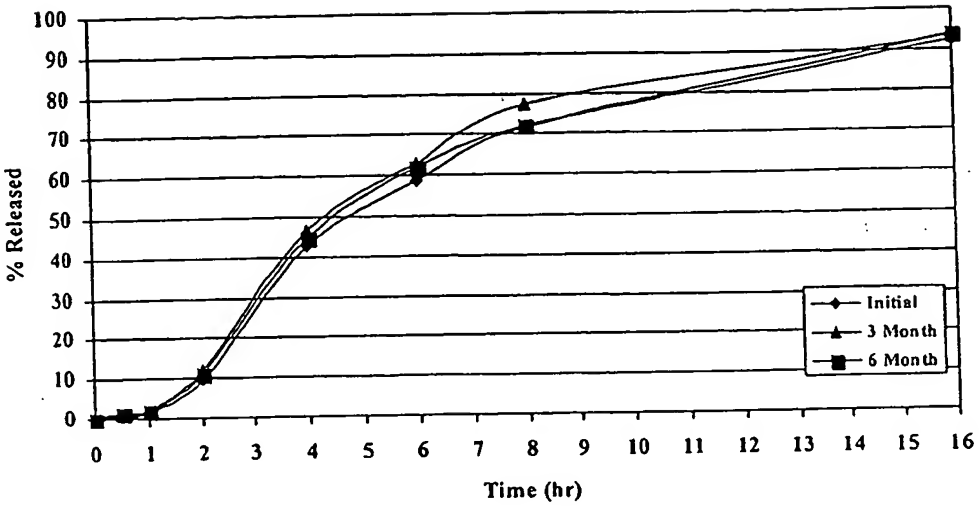
% Released
Time (hr)
Initial
3 Month
6 Month

FIG. 3

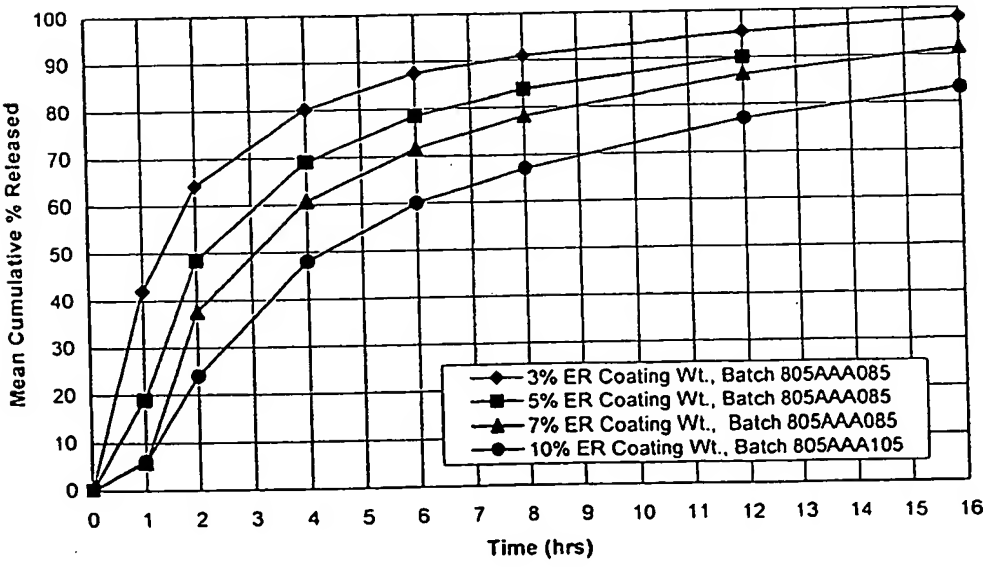
Mean Cumulative % Released
Time (hrs)
3% ER Coating Wt., Batch 805AAA085
5% ER Coating Wt., Batch 805AAA085
7% ER Coating Wt., Batch 805AAA085
10% ER Coating Wt., Batch 805AAA105

FIG. 4

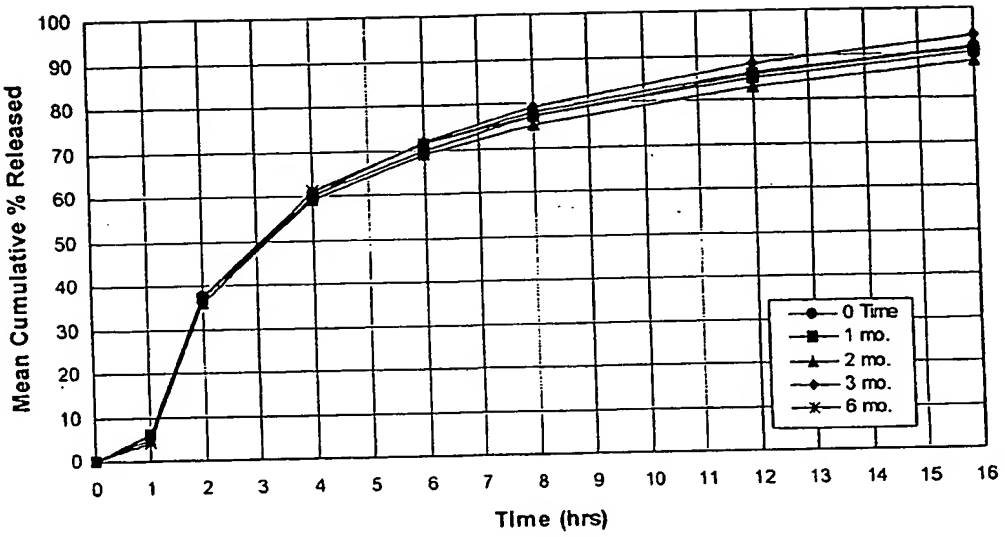
Mean Cumulative % Released
Time (hrs)
0 Time
1 mo.
2 mo.
3 mo.
6 mo.

FIG. 5

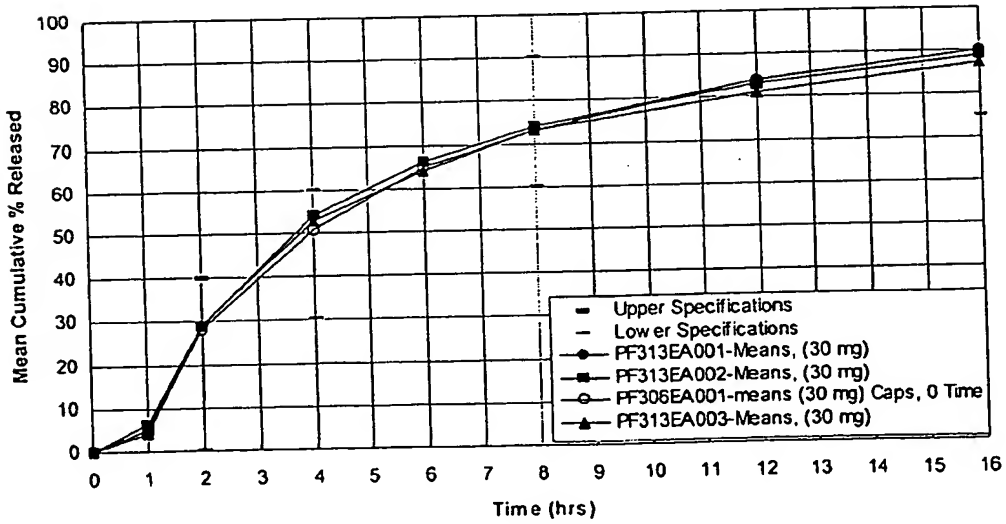
Mean Cumulative % Released
Time (hrs)
Upper Specifications
Lower Specifications
PF313EA001-Means, (30 mg)
PF313EA002-Means, (30 mg)
PF306EA001-means (30 mg) Caps, 0 Time
PF313EA003-Means, (30 mg)

FIG. 6

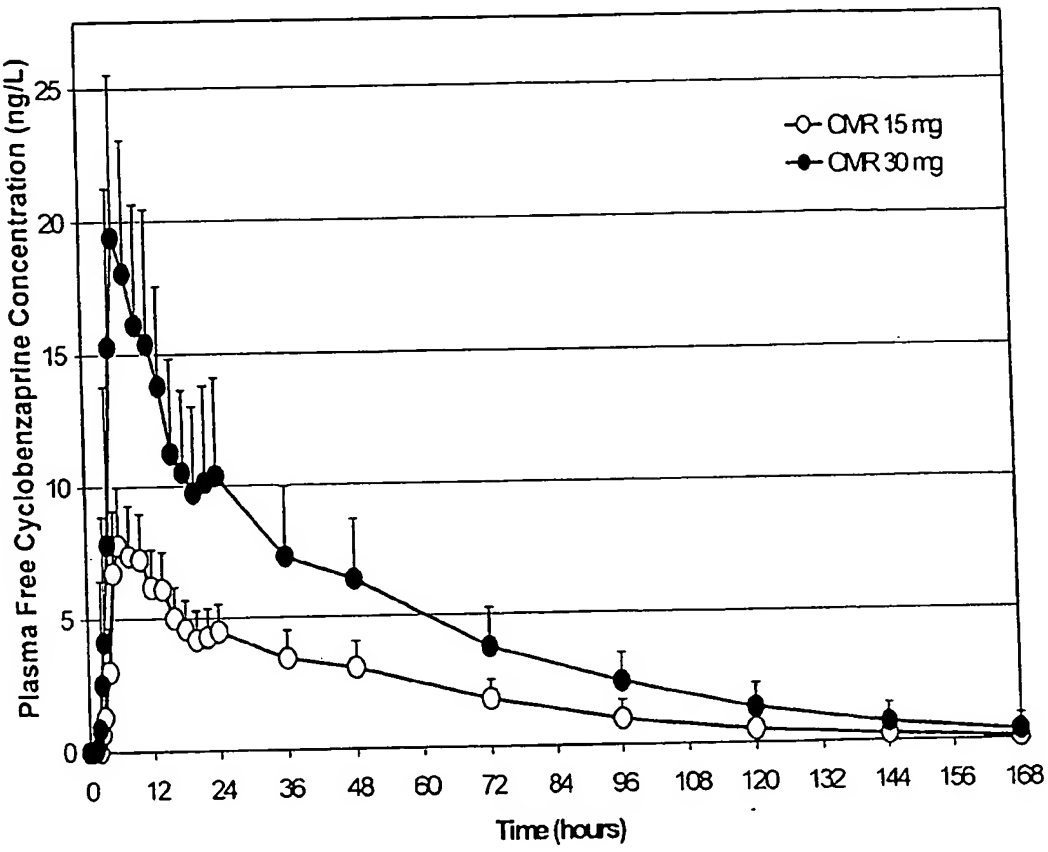
Plasma Free Cyclobenzaprine Concentration (ng/L)
0
5
10
15
20
25
0
12
24
36
48
60
72
84
96
108
120
132
144
156
168
Time (hours)
CMR 15 mg
CMR 30 mg

FIG. 7

MODIFIED RELEASE DOSAGE FORMS OF SKELETAL MUSCLE RELAXANTS

TECHNICAL FIELD

A major objective of developing and commercializing controlled release dosage forms for indications such as cardiovascular diseases, chronic pain, relief of muscle spasm and associated symptoms especially in the elderly is to deliver the drug so as to maintain the drug at therapeutically effective concentrations over an extended period of time, thereby enhancing patient compliance and therapeutic efficacy, thereby reducing both cost of treatment and side effects.

BACKGROUND OF THE INVENTION

Many therapeutic agents are most effective when made available at a constant rate at or near the absorption site. The absorption of therapeutic agents thus made available generally results in desired plasma concentrations leading to maximum efficacy and minimum toxic side effects. Much effort has been devoted to developing matrix tablet based and multi-particulate capsule based drug delivery systems for oral applications.

U.S. Pat. No. 4,839,177 to Colombo, et al, assigned to Jagotec AG, refers broadly to controlled release of active substances including medicaments and any type of substance which is to be released at a controlled rate into an aqueous fluid. The patent is directed to a system for the controlled-rate release of active substances consisting of a deposit core comprising an active substance and at least one of (a) a polymeric material having a high degree of swelling on contact with water and a gellable polymeric material or (b) a single polymeric material having both swelling and gelling properties, and a support platform applied to the deposit core wherein the support platform consists of a water insoluble polymeric material.

U.S. Pat. Nos. 4,851,228 and No. 4,968,507, both to Zentner et al., assigned to Merck & Company, refer to a multi-particulate osmotic pump for the controlled release of a pharmaceutically active agent, each osmotic pump element consisting essentially of a core containing an active agent and a rate controlling water insoluble wall comprising a semi-permeable polymer and at least one pH insensitive pore forming additive dispersed throughout the wall. U.S. Pat. No. 4,590,062 to Jang assigned to Tech Trade Corporation and U.S. Pat. No. 4,882,167 to Jang, are directed to a compressed product containing an active produced by dry blending with a matrix combination of a hydrophobic polymer (e.g. ethylcellulose) and a wax, fatty acid, neutral lipid or combination thereof.

U.S. Pat. No. 4,996,047 to Kelleher, assigned to Richardson-Vicks, is directed to an oral pharmaceutical composition in unit dosage form of ion-exchange resin particles having a pharmacologically active drug bound thereto wherein the drug-resin complex particles have been coated with a water-impermeable diffusion barrier to provide controlled release of the active drug. U.S. Pat. No. 5,120,548 to McClelland et al., assigned to Merck & Company, is directed to a controlled release drug delivery device comprising a composition of a polymer which swells upon exposure to an aqueous environment, a plurality of controlled release swelling modulators, at least one active agent and either a water insoluble polymer coating surrounding the composition or a microporous wall surrounding the composition. U.S. Pat. No. 5,350,584 to McClelland et al., assigned to Merck & Company, relates to a process for the production of microcrystalline cellulose-free multiparticulates comprising a medicament and a charged resin. The resulting spheronized beads can be used in certain controlled release dosage forms.

U.S. Pat. No. 5,366,738 to Rork et al., assigned to Merck & Company, is directed to a drug delivery device for controlled release of an active agent. The drug delivery device includes a compressed core with an active agent and a polymer which forms gelatinous microscopic particles upon hydration and a water insoluble, water impermeable polymeric coating comprising a polymer and plasticizer which surrounds and adheres to the core.

U.S. Pat. No. 5,582,838 to Rork et al., assigned to Merck & Company, is related to a drug delivery device for the controlled release of a beneficial agent. The drug delivery device includes a compressed core having at least two layers: at least one layer is a mixture of a beneficial agent and a polymer which forms microscopic polymer gel beads upon hydration and at least one outer layer comprises a polymer which forms microscopic polymer gel beads upon hydration. A water insoluble, water impermeable coating is applied to the core and the coating has apertures exposing between about 5-75% of the core surface.

U.S. Pat. No. 5,874,418 to Stella et al., assigned to Cydex, is directed to a pharmaceutical composition comprising a carrier and a mixture of a sulfoalkyl ether-cyclodextrin and a therapeutic agent wherein a major portion of the therapeutic agent is not complexed to the sulfoalkyl ether-cyclodextrin derivative. Delayed, sustained or controlled release formulations are also described wherein the pharmaceutical core is coated with a film coating comprising a file forming agent and a pore forming agent. U.S. Pat. No. 5,882,682 to Rork et al., assigned to Merck & Company, is directed to a drug delivery process including the steps of preparing a uniform mixture of a polymer which forms gelatinous microscopic particles upon hydration, the beneficial agent and other excipients used in the preparation of the core; compressing the mixture into cores; coating the entire core with a water insoluble, water impermeable polymeric coating including a polymer and a plasticizer; and forming apertures through the coating.

U.S. Pat. No. 5,952,451 to Zhao, assigned to Guilford Pharmaceuticals is directed to a process for preparing high molecular weight poly(phosphoester) compositions comprising a biologically active substance and a poly(phosphoester) and the high molecular weight compositions produced thereby. The polymers so produced are useful in prolonged released drug delivery systems. U.S. Pat. No. 6,004,582 to Faour et al., assigned to Laboratorios Phoenix U.S.A., is directed to a multi-layered osmotic device comprising a compressed core including a first active agent and an osmotic agent, a semi-permeable membrane surrounding the core and having a preformed passageway therein wherein the membrane is permeable to a fluid in the environment of use and substantially impermeable to the first active agent. The semi-permeable membrane preferably consists essentially of cellulose acetate and poly(ethylene glycol). The external coat can includes poly(vinylpyrrolidone) and poly (ethylene glycol) and can further includes materials such as HPMC, ethylcellulose, hydroxyl ethylcellulose, CMC, dimethylaminoethyl methacrylate-methacrylic acid ester copolymer, ethyl acrylate-methyl methacrylate copolymer, and combinations thereof.

WO 99/18937 to Kleinbart et al., (Merck & Company), is directed to a composition comprising a pharmaceutically effective amount of cyclobenzaprine and calcium phosphate dibasic hydrous, wherein the tablet releases most of the

active component within an hour. WO 99/30671 to Ron, is directed to an oral delivery vehicle including an aspected particle comprising a pharmaceutically active component and excipients wherein the vehicle is formulated to provide controlled delivery of the pharmaceutically active component. The vehicle may further contain a coating to provide sustained drug delivery to the particle. WO 98/53802 to Faour et al., (Laboratorios Phoenix USA), is directed to a multi-layered osmotic device that is capable of delivering a first active agent in an outer lamina to one environment of use and a second active agent in the core to another environment of use. An erodible polymer coat between an internal semipermeable membrane and a second active agent-containing external coat comprises poly(vinylpyrrolidone)-vinyl acetate) copolymer. The active agent in the core is delivered through a pore containing an erodible plug.

WO 98/18610 to Van Lengerich, is directed to particles containing an active agent, which provide controlled release of the active ingredient without substantial destruction of the matrix material. A release-rate controlling component is incorporated in a matrix to control the rate-release of the encapsulant from the particles. A hydrophobic component or a high water binding capacity component may be used for extending the release time. Release properties may also be controlled by precoating the encapsulant and/or coating the particles with a film-forming component. WO 98/06439 to Oedemoed, (Osteotech), is directed to a composition comprising a biologically active agent encapsulated in a matrix comprising a polyether ester copolymer, such as polyethylene glycol terephthalate/polybutylene-terephthalate copolymer. The polyether ester copolymer protects the active agent from degradation and thereby facilitates the drug delivery.

Cyclobenzaprine hydrochloride, a skeletal muscle relaxant, is a centrally acting drug which reduces or abolishes excessive tonic muscle activity in hypertonic as opposed to hyperphasic disorders. Flexeril IR (immediate release) tablets containing 10 mg of cyclobenzaprine HCl are administered three times a day to relieve skeletal muscle spasm of local origin without interfering with muscle function. The oral administration thrice daily is an issue of patient compliance, especially with the elderly. Hence, there is a need for modified release skeletal muscle relaxant suitable for a single administration. More particularly, there is a need for modified release (MR) cyclobenzaprine hydrochloride capsules, 15 and 30 mg, which would substantially minimize intersubject variability and improve the quality of life, especially in the elderly population.

SUMMARY OF THE INVENTION

The present invention provides a modified release, multiparticulate dosage form of a skeletal muscle relaxant comprising one or more bead populations which provides an extended release profile of the active under in vitro conditions closely mimicking the profile simulated from pharmaco-kinetic modeling. One of the bead populations is an ER (extended release) Bead population typically comprising a coating of a water insoluble polymer alone, or in combination with a water soluble polymer, applied onto active containing cores. The active core of the dosage form of the present invention may comprise an inert particle such as a sugar sphere, or an acidic or alkaline buffer crystal, which is coated with a skeletal muscle relaxant such as cyclobenzaprine hydrochloride-containing film-forming formulation, preferably a water-soluble film forming composition. The first coating formulation may contain, in addition to the active, a binder such as hydroxypropyl cellulose. The drug layered beads may be coated with a protective seal coating of OPADRY® Clear to produce IR Beads. Alternatively, the core particle may be formed by granulating and dry milling and/or by extrusion and spheronization of a pharmaceutical composition containing the active. The amount of drug in the core will depend on the dose required and typically varies from about 5 to about 60% by weight.

ER Beads can be produced by applying a functional membrane comprising a water insoluble polymer alone or in combination with a water soluble polymer onto IR Beads. The capsule formulation for once a day, oral administration of a skeletal muscle relaxant prepared in accordance with the present invention comprises ER Beads containing the active substance and optionally IR Beads. IR (immediate release) Beads allow immediate release of the active while ER Beads allow an extended release profile of the active over several hours. Upon oral administration, such a capsule formulation provides for therapeutically effective plasma profiles over an extended period of time, thereby resulting in improved patient compliance.

In accordance with one embodiment of the invention a pharmaceutical dosage form of a skeletal muscle relaxant is provided. The dosage form includes one or more bead populations and provides a modified release profile. At least one of the bead populations includes extended release (ER) beads wherein the ER beads include a core particle (IR (immediate release) bead) containing a skeletal muscle relaxant and an ER (extended release) coating comprising a water insoluble polymer surrounding the core. The dosage form, in accordance with certain embodiments, when dissolution tested using United States Pharmacopoeia Apparatus 2 (paddles @ 50 rpm) in 900 mL of 0.1N HCl (or a suitable dissolution medium) at 37° C. exhibits a drug release profile substantially corresponding to the following pattern:

- after 2 hours, no more than about 40% of the total active is released;
- after 4 hours, from about 40-65% of the total active is released;
- after 8 hours, from about 60-85% of the total active is released; and
- after 12 hours, from about 75-85% of the total active is released.

The dosage form thereby provides a therapeutically effective plasma concentration over an extended period of time, typically over a period of 24 hours to treat muscle spasm associated with painful musculoskeletal conditions in humans.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described in further detail with reference to the accompanying Figures wherein:

FIG. 1 shows the proposed target release profile for cyclobenzaprine hydrochloride MR (modified release) capsules, 15 and 30 mg.

FIG. 2 shows the simulated Day 1 plasma level following dosing of 1×10 mg Flexeril® given 3 times a day and 1×10 mg cyclobenzaprine HCl MR capsule given once-daily.

FIG. 3 shows the drug release profiles for cyclobenzaprine HCl ER (extended release) beads of Example 2.

FIG. 4 compares the drug release profiles as a function of membrane coating of Example 3.

FIG. 5 shows the drug release profiles for cyclobenzaprine HCl ER beads of Example 3 stored in induction sealed HDPE bottles on accelerated stability.

FIG. 6 shows the drug release profiles for 30 mg cyclobenzaprine HCl MR capsules of Example 4.

FIG. 7 shows the plasma levels for cyclobenzaprine HCl MR capsules, 15 and 30 mg of Example 5.

DETAILED DESCRIPTION OF THE INVENTION

All documents cited are, in relevant part, incorporated herein by reference; the citation of any document is not to be construed as an admission that it is prior art with respect to the present invention.

The active core of the dosage form of the present invention may be comprised of an inert particle or an acidic or alkaline buffer crystal, which is coated with a drug-containing film-forming formulation and preferably a water-soluble film forming composition to form a water-soluble/dispersible particle. Alternatively, the active may be prepared by granulating and milling and/or by extrusion and spheronization of a polymer composition containing the drug substance. The amount of drug in the core will depend on the dose that is required, and typically varies from about 5 to 60 weight %. Generally, the polymeric coating on the active core will be from about 4 to 20% based on the weight of the coated particle, depending on the type of release profile required and/or the polymers and coating solvents chosen. Those skilled in the art will be able to select an appropriate amount of drug for coating onto or incorporating into the core to achieve the desired dosage. In one embodiment, the inactive core may be a sugar sphere or a buffer crystal or an encapsulated buffer crystal such as calcium carbonate, sodium bicarbonate, fumaric acid, tartaric acid, etc. which alters the microenvironment of the drug to facilitate its release.

The drug-containing particle may be coated with an extended release (ER) coating comprising a water insoluble polymer or a combination of a water insoluble polymer and a water soluble polymer to provide ER beads. In accordance with certain embodiments, the water insoluble polymer and the water soluble polymer may be present at a weight ratio of from 100/0 to 65/35, more particularly from about 95/5 to 70/30, and still more particularly at a ratio of from about 85/15 to 75/25. The extended release coating is applied in an amount necessary to provide the desired release profile. The extended release coating typically comprises from about 1% to 15%, more particularly from about 7% to 12%, by weight of the coated beads.

The present invention also provides a method of making a modified release dosage form including a mixture of two bead populations. In accordance with one embodiment, the method includes the steps of:

1. preparing a drug-containing core by coating an inert particle such as a non-pareil seed, an acidic buffer crystal or an alkaline buffer crystal with a drug and a polymeric binder or by granulation and milling or by extrusion/spheronization to form an immediate release (IR) bead;
2. coating the IR bead with a plasticized water-insoluble polymer alone such as ethylcellulose or in combination with a water soluble polymer such as hydroxypropylmethylcellulose to form an Extended Release (ER) bead;
3. filling into hard gelatin capsules ER Beads alone or in combination with IR Beads at a proper ratio to produce MR (modified release) capsules providing the desired release profile.

IR beads when tested in accordance with the following procedure release at least about 70%, more specifically at least about 90% of the active within 30 minutes.

Dissolution Procedure:

Dissolution Apparatus: USP Apparatus 2 (Paddles at 50 rpm), dissolution medium: 900 mL 0.1N HCl (or a suitable dissolution medium) at 37° C. and Drug Release determination by HPLC).

An aqueous or a pharmaceutically acceptable solvent medium may be used for preparing drug-containing core particles. The type of film forming binder that is used to bind the drug to the inert sugar sphere is not critical but usually water soluble, alcohol soluble or acetone/water soluble binders are used. Binders such as polyvinylpyrrolidone (PVP), polyethylene oxide, hydroxypropyl methylcellulose (HPMC), hydroxypropylcellulose (HPC), polysaccharides such as dextran, corn starch may be used at concentrations from about 0.5 to 5 weight %, although other concentrations may be useful. The drug substance may be present in this coating formulation in the solution form or may be dispersed at a solid content up to about 35 weight % depending on the viscosity of the coating formulation.

In accordance with certain embodiments, the drug substance, optionally a binder such as PVP, a dissolution rate controlling polymer (if used), and optionally other pharmaceutically acceptable excipients are blended together in a planetary mixer or a high shear granulator such as Fielder and granulated by adding/spraying a granulating fluid such as water or alcohol. The wet mass can be extruded and spheronized to produce spherical particles (beads) using an extruder/marumerizer. In these embodiments, the drug load could be as high as 90% by weight based on the total weight of the extruded/spheronized core.

Representative muscle relaxants include cyclobenzaprine, dantrolene sodium, methocarbamol, metaxalone, carisoprodol, diazepam and pharmaceutically acceptable salts or derivatives thereof. Cyclobenzaprine hydrochloride is a particularly useful muscle relaxant. As used herein, the useful muscle relaxants include the base, pharmaceutically acceptable salts thereof such as hydrochloride, stereoisomers thereof and mixtures thereof.

Representative examples of water insoluble polymers useful in the ER coating include ethylcellulose powder or an aqueous dispersion (such as AQUACOAT® ECD-30), cellulose acetate, polyvinyl acetate (Kollicoat SR#30D from BASF), neutral copolymers based on ethyl acrylate and methylmethacrylate, copolymers of acrylic and methacrylic acid esters with quaternary ammonium groups such as Eudragit NE, RS and RS30D, RL or RL30D and the like. Representative examples of water soluble polymers useful herein include low molecular weight hydroxypropyl methylcellulose (HPMC), methylcellulose, hydroxypropylcellulose, polyvinylpyrrolidone, polyethylene glycol (PEG of molecular weight>3000) and mixtures thereof. The extended release coating will typically be applied at a thickness ranging from about 1 weight % up to 15 weight % depending on the solubility of the active in water and the solvent or latex suspension based coating formulation used.

The coating compositions used in forming the membranes are usually plasticized. Representative examples of plasticizers that may be used to plasticize the membranes include triacetin, tributyl citrate, triethyl citrate, acetyl tri-n-butyl citrate diethyl phthalate, polyethylene glycol, polypropylene glycol, castor oil, dibutyl sebacate, acetylated monoglycerides and the like or mixtures thereof. The plasticizer may comprise about 3 to 30 wt. % and more typically about 10 to 25 wt. % based on the polymer. The type of plasticizer and

its content depends on the polymer or polymers, nature of the coating system (e.g., aqueous or solvent based, solution or dispersion based and the total solids).

In general, it is desirable to prime the surface of the particle before applying an extended release membrane coating or to separate the different membrane layers by applying a thin hydroxypropyl methylcellulose (HPMC)(OPADRY® Clear) film. While HPMC is typically used, other primers such as hydroxypropylcellulose (HPC) can also be used.

The membrane coatings can be applied to the core using any of the coating techniques commonly used in the pharmaceutical industry, but fluid bed coating is particularly useful.

The present invention is applied to multi-dose forms, i.e., drug products in the form of multi-particulate dosage forms (pellets, beads, granules or mini-tablets) or in other forms suitable for oral administration. As used herein, these terms are used interchangeably to refer to multi-particulate dosage forms.

The invention also provides a method of making an extended release dosage form which includes a mixture of two or more bead populations. In accordance with one aspect of the present invention, the method includes the steps of:

(a) coating an inert particle such as a non-pareil seed, an acidic buffer crystal or an alkaline buffer crystal with a drug and polymeric binder to form an active drug particle (IR beads), which may be present in the unit dosage form to act as a bolus dose;

(b) coating the active drug particle with a solution or suspension of a water insoluble polymer or a mixture of water soluble and water insoluble polymers to form an extended release coated drug particle (ER beads);

(c) filling into a hard gelatin capsule ER beads alone and optionally, in combination with IR beads at a proper ratio ranging from 95/5 to 70/30 (ER beads/IR beads) to produce a MR (modified release) capsule exhibiting a target drug release profile.

The following non-limiting examples illustrate the capsule dosage forms manufactured in accordance with the invention using cyclobenzaprine hydrochloride as a test case, which exhibit in vitro drug release profiles, similar to that predicted by performing modeling exercises. Such dosage forms when orally administered, would enable maintaining drug plasma concentrations at therapeutically effective levels over extended periods of time, thereby significantly improving patient compliance.

EXAMPLE 1

Cyclobenzaprine is well absorbed after oral administration, but there is a large intersubject variation in plasma levels. It is eliminated quite slowly with a half-life as long as one to three days. The present treatment regimen of 10 mg three times daily is an issue of patient compliance, especially the elderly. Hence, a modified release dosage form (capsule) was designed with a release profile shown in FIG. 1. To determine if this is the proper release profile, the pharmacokinetics data of cyclobenzaprine following a single dose of 10 mg Flexeril® tablets administered 3 times a day was taken from the literature. A pharmacokinetic model was developed from this data using WinNonlin™ Version 1.5.

The resulting model parameters are listed below:

Model Parameter	Value
Volume of Distribution/F	429 L
K01	0.2031 hr^{-1}
K10	0.1004 hr^{-1}
K12	0.0828 hr^{-1}
K21	0.0398 hr^{-1}
Tlag	0 hr
Dose	2 x 10 mg Tablets

Theoretical plasma levels were simulated using the pharmacokinetic model given above and the target release rate given in FIG. 1. FIG. 2 shows the simulated plasma levels for day one following dosing of 1×10 mg Flexeril® Tablet given 3 times a day and the proposed Cyclobenzaprine HCl MR Capsule, 30 mg given once a day.

EXAMPLE 2

Cyclobenzaprine Hydrochloride (1,200 g) was slowly added to an aqueous solution of polyvinylpyrrolidone such as Povidone USP (K-29/32, 80 g) and mixed well. # 25-30 mesh sugar spheres (2,640 g) were coated with the drug solution in a Glatt fluid bed coater, equipped with a 9" bottom spray Wurster insert to provide IR beads with a coating weight of about 9%. The drug containing particles were dried, and a seal coat of OPADRY® Clear (2% w/w) was first applied and dried in the Glatt fluid bed unit as a precautionary measure to drive off excessive surface moisture. The composition and batch quantities of the IR Beads were given in 5 to 10 kg. Following the second coating process the IR Beads were passed through 14 and 25 mesh screens. Beads remaining on the 14-mesh screen were discarded as oversized beads and beads passing through the 25-mesh screen were discarded as undersized beads.

The next step in the process was to apply an extended release polymer membrane by spraying AQUACOAT® ECD 30, an aqueous dispersion of ethylcellulose with dibutyl sebacate (76:24), onto the IR Beads for a weight gain of approximately 10%. The same fluid bed equipment was used to produce ER (extended release) Beads by further coating the AQUACOAT® coated beads with OPADRY® Clear for a weight gain of 2% w/w prior to curing at 60° C. in a conventional oven for a period of 24 hours. The batch size was 5 to 10 kg. The drug release profiles are shown in FIG. 3. The figure also shows the drug release profiles from ER Beads stored in induction sealed HDPE bottles at 25° C./60% RH for 6 months.

EXAMPLE 3

Cyclobenzaprine Hydrochloride (2.5 kg) was dissolved in 50/50 acetone/purified water. 25-30 mesh Sugar spheres, (7.3 kg) were coated with the drug solution in a Glatt fluid bed coater, equipped with a 9" bottom spray Wurster insert. The drug containing particles were dried, and a seal coat of OPADRY® Clear (2% w/w) was first applied and dried in the Glatt fluid bed unit as a precautionary measure to drive off excessive surface moisture. 910 g of ethylcellulose (Ethocel Premium Standard 10 cps) and 90 g of diethyl phthalate were dissolved in 98/02 acetone/purified water and applied onto the IR Beads (9 kg) in the Glatt GPCG 5 in accordance with the present invention. The release rates of the ER Beads will vary depending upon the film weight of the ER coating. One

batch of IR Beads was coated for a final weight gain of 7% based on the weight of coated beads wherein samples of the ER Beads were removed during the ER coating process to yield beads with increasing coating weights. Another batch was coated for 10% weight gain and all the coated bead batches were cured at 60° C. for 4 hours in a conventional oven. FIG. 4 shows the relationship between the ER coating weights and the release rate of the finished ER coated Beads.

A batch was coated with a 7% ER coating and cured at 60° C. for 4 hours. No changes were noted in the release rates, assay values or impurity levels after storage in HDPE bottles at 40° C./75% RH for a period of 6 months. The release rates for the samples are shown in FIG. 5.

EXAMPLE 4

The drug layering, seal coating, and ER Coating processes were scaled-up to Glatt GPCG 120 equipped with an 18" bottom spray Wurster insert (batch size: 80 kg for IR Beads and 85 kg for ER Beads). The process parameters of each of the processes were optimized. The drug layering solution (9% weight gain), seal coating solution, and the ER coating solution (9% weight gain) were sprayed onto the sugar spheres or IR Beads while maintaining the product temperature between narrow limits. Following the seal or ER coating the beads were passed through 14 and 25 mesh screens discarding any beads remaining on the 14 mesh screen. The ER Beads were also cured at 60° C. for a period of 4 hours. The Extended Release Beads were then filled into size 4 capsules to produce Cyclobenzaprine HCl MR Capsules, 15 and 30 mg. The drug release profiles of 30 mg capsules of one pivotal clinical and three registration stability batches are presented in FIG. 6.

EXAMPLE 5

A Randomized double-blind two-period crossover study to assess the safety and bioavailability of Cyclobenzaprine HCl Modified-release (CMR) 15 mg and 30 mg in healthy male and female volunteers (N=14 or 15) was performed. Each subject received one 15 mg or 30 mg capsule of CMR in the morning, separated by a 14-day washout period between doses. The results are presented in Table 1 and FIG. 7 wherein $AUC_{0\text{-}168}$ refers to the area under the plasma concentration-time curve to the last measurable time point (168 hrs) calculated by the linear trapezoidal rule, $AUC_{0\text{-}\infty}$ refers to area under the concentration-time curve to infinity, C_{max} refers to the maximum blood plasma concentration and T_{max} refers to the time to maximum plasma levels of cyclobenzaprine.

TABLE 1

Pharmacokinetic Results: Mean (±SD) pharmacokinetic parameters are presented for subjects in the Safety population in the following table

	CMR 15 mg N = 15	CMR 30 mg N = 14
$AUC_{0\text{-}168}$ (ng · hr/mL)	318.30 ± 114.657	736.60 ± 259.414
$AUC_{0\text{-}\infty}$ (ng · hr/mL)	354.075 ± 119.8037	779.889 ± 277.6349
C_{max} (ng/mL)	8.315 ± 2.1635	19.851 ± 5.8765
Time to Peak, T_{max} (hr)	8.1 ± 2.94	7.1 ± 1.59
Elimination Half-life, $t_{1/2}$ (hr)	33.401 ± 10.2882	31.977 ± 10.1310

The treatments were significantly different from each other as values for AUCs and C_{max} were higher for CMR 30 mg than those for CMR 15 mg. The bioavailability of CMR 30 mg was approximately twice that of CMR 15 mg as shown by the AUCs. The adjusted mean ratio of CMR 30 mg to CMR 15 mg was greater than about 2 for each of the AUCs and C_{max}, specifically the calculated values were 2.42 for $AUC_{0\text{-}168}$ ($p<0.001$), 2.286 for $AUC_{0\text{-}\infty}$ ($p<0.001$), and 2.424 for C_{max} ($p<0.001$). Overall, both CMR 15 mg and 30 mg were well tolerated during the study.

Accordingly, one aspect of the invention relates to a dosage form containing cyclobenzaprine hydrochloride as a skeletal muscle relaxant wherein the pharmaceutical dosage form provides a maximum blood plasma concentration (C_{max}) within the range of about 80% to 125% of about 20 ng/mL of cyclobenzaprine HCl, an $AUC_{0\text{-}168}$ within the range of about 80% to 125% of about 740 ng·hr/mL and a T_{max} within the range of about 80% to 125% of about 7 hours following oral administration of a single 30 mg cyclobenzaprine HCl MR Capsule.

While the invention has been described in detail and with reference to specific examples thereof, it will be apparent to one skilled in the art that various changes and modifications can be made without departing from the spirit and scope thereof.

What is claimed is:

1. A multi-particulate pharmaceutical dosage form of a skeletal muscle relaxant providing a modified release profile comprising a population of extended release beads,

wherein said extended release beads comprise

an active-containing core particle comprising a skeletal muscle relaxant selected from the group consisting of cyclobenzaprine, pharmaceutically acceptable salts or derivatives thereof and mixtures thereof; and

an extended release coating comprising a water insoluble polymer membrane surrounding said core,

wherein said dosage form when dissolution tested using United States Pharmacopoeia Apparatus 2 (paddles @ 50 rpm) in 900 mL of 0.1N HCl at 37° C. exhibits a drug release profile substantially corresponding to the following pattern:

after 2 hours, no more than about 40% of the total active is released;

after 4 hours, from about 40-65% of the total active is released

after 8 hours, from about 60-85% of the total active is released;

wherein said dosage form provides therapeutically effective plasma concentration over a period of 24 hours to treat muscle spasm associated with painful musculoskeletal conditions when administered to a patient in need thereof; and

wherein said water insoluble polymer membrane comprises a water insoluble polymer selected from the group consisting of ethers of cellulose, esters of cellulose, cellulose acetate, ethyl cellulose, polyvinyl acetate, neutral copolymers based on ethylacrylate and methylmethacrylate, copolymers of acrylic and methacrylic acid esters with quaternary ammonium groups, pH-insensitive ammonio methacrylic acid copolymers, and mixtures thereof; and a plasticizer selected from the group consisting of triacetin, tributyl citrate, tri-ethyl citrate, acetyl tri-n-butyl citrate, diethyl phthalate, dibutyl sebacate, polyethylene glycol, polypropylene glycol, castor oil, acetylated mono- and di-glycerides and mixtures thereof.

2. The pharmaceutical dosage form of claim 1, wherein said skeletal muscle relaxant comprises cyclobenzaprine hydrochloride.

3. The pharmaceutical dosage form of claim 2 wherein said pharmaceutical dosage form provides a maximum blood plasma concentration (C_{max}) within the range of about 80% to

125% of about 20 ng/mL of cyclobenzapnine HCl and an AUC_{0-168} within the range of about 80% to 125% of about 740 ng·hr/mL and a T_{max} within the range of 80% to 125% of about 7 hours following oral administration of a single 30 mg cyclobenzapnine HCl MR Capsule.

4. The pharmaceutical dosage form of claim 3 wherein the adjusted mean ratio of CMR 30 mg/CMR 15 mg is greater than about 2 for each of AUC_{0-168} ($p<0.001$), $AUC_{0-\infty}$ ($p<0.001$), and C_{max} ($p<0.001$).

5. The pharmaceutical dosage form of claim 1, wherein said dosage form comprises only one extended release bead population.

6. The pharmaceutical dosage form of claim 1, wherein said water insoluble polymer membrane on the drug cores comprises from about 7% to 12% by weight of the extended release beads.

7. The pharmaceutical dosage form of claim 1, wherein said extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

8. The pharmaceutical dosage form of claim 1, wherein said skeletal muscle relaxant comprises cyclobeuzaprine.

9. The pharmaceutical dosage form of claim 1, wherein said drug release profile substantially corresponds to the following pattern:

after 2 hours, no more than about 40% of the total active is released;

after 4 hours, from about 40-65% of the total active is released;

after 8 hours, from about 60-85% of the total active is released; and

after 12 hours, from about 75-85% of the total active is released.

10. The pharmaceutical dosage form of claim 1, wherein said extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

11. The pharmaceutical dosage form of claim 1, wherein the water insoluble polymer membrane comprises ethyl cellulose.

12. The pharmaceutical dosage form of claim 11, wherein said plasticizer is diethyl phthalate.

13. The pharmaceutical dosage form of claim 11, wherein the extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

14. The pharmaceutical dosage form of claim 12, wherein the extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

15. The pharmaceutical dosage form of claim 14, wherein the water soluble polymer is hydroxypropyl methylcellulose.

16. The pharmaceutical dosage form of claim 15, wherein the skeletal muscle relaxant is cyclobenzaprine hydrochloride.

17. The pharmaceutical dosage form of claim 16, wherein the water insoluble polymer membrane comprises from about 7% to 12% by weight of the extended release beads.

18. The pharmaceutical dosage form of claim 17, wherein the drug release profile substantially corresponds to the following pattern:

after 2 hours, no more than about 40% of the total active is released;

after 4 hours, from about 40-65% of the total active is released;

after 8 hours, from about 60-85% of the total active is released; and

after 12 hours, from about 75-85% of the total active is released.

19. The pharmaceutical dosage form of claim 1, wherein said water insoluble polymer membrane comprises a water insoluble polymer selected from the group consisting of ethers of cellulose, esters of cellulose, pH-insensitive ammonio methacrylic acid copolymers, and mixtures thereof.

20. The pharmaceutical dosage form of claim 19, wherein said extended release coating further comprises a water soluble polymer selected from the group consisting of methylcellulose, hydroxypropylcellulose, hydroxypropyl methylcellulose, polyethylene glycol polyvinylpyrrolidone and mixtures thereof.

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Exhibit B

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

WYETH, *et al.*,

Plaintiffs,

v.

JON W. DUDAS, Under Secretary of Commerce for Intellectual Property and Director of U.S. Patent and Trademark Office,

Defendant.

Civil Action No. 07-1492 (JR)

MEMORANDUM OPINION

Plaintiffs here take issue with the interpretation that the United States Patent and Trademark Office (PTO) has imposed upon 35 U.S.C. § 154, the statute that prescribes patent terms. Section 154(a)(2) establishes a term of 20 years from the day on which a successful patent application is first filed. Because the clock begins to run on this filing date, and not on the day the patent is actually granted, some of the effective term of a patent is consumed by the time it takes to prosecute the application. To mitigate the damage that bureaucracy can do to inventors, the statute grants extensions of patent terms for certain specified kinds of PTO delay, 35 U.S.C. § 154(b)(1)(A), and, regardless of the reason, whenever the patent prosecution takes more than three years. 35 U.S.C. § 154(b)(1)(B). Recognizing that the protection provided by these separate guarantees might overlap, Congress has forbidden double-counting: "To the extent that periods of delay attributable to grounds

specified in paragraph (1) overlap, the period of any adjustment granted under this subsection shall not exceed the actual number of days the issuance of the patent was delayed." 35 U.S.C. § 154(b)(2)(A). Plaintiffs claim that the PTO has misconstrued or misapplied this provision, and that the PTO is denying them a portion of the term Congress has provided for the protection of their intellectual property rights.

Statutory Scheme

Until 1994, patent terms were 17 years from the date of issuance. See 35 U.S.C. § 154 (1992) ("Every patent shall contain . . . a grant . . . for the term of seventeen years . . . of the right to exclude others from making, using, or selling the invention throughout the United States. . . ."). In 1994, in order to comply with treaty obligations under the General Agreement on Tarriffs and Trade (GATT), the statute was amended to provide a 20-year term from the date on which the application is first filed. See Pub. L. No. 103-465, § 532, 108 Stat. 4809, 4984 (1994). In 1999, concerned that extended prosecution delays could deny inventors substantial portions of their effective patent terms under the new regime, Congress enacted the American Inventors Protection Act, a portion of which -- referred to as the Patent Term Guarantee Act of 1999 -- provided for the adjustments that are at issue in this case. Pub. L. No. 106-113, §§ 4401-4402, 113 Stat. 1501, 1501A-557 (1999).

As currently codified, 35 U.S.C. § 154(b) provides three guarantees of patent term, two of which are at issue here. The first is found in subsection (b)(1)(A), the "[g]uarantee of prompt Patent and Trademark Office response." It provides a one-day extension of patent term for every day that issuance of a patent is delayed by a failure of the PTO to comply with various enumerated statutory deadlines: fourteen months for a first office action; four months to respond to a reply; four months to issue a patent after the fee is paid; and the like. See 35 U.S.C. § 154(b)(1)(A)(i)-(iv). Periods of delay that fit under this provision are called "A delays" or "A periods." The second provision is the "[g]uarantee of no more than 3-year application pendency." Under this provision, a one-day term extension is granted for every day greater than three years after the filing date that it takes for the patent to issue, regardless of whether the delay is the fault of the PTO.[1] See 35 U.S.C. § 154(b)(1)(B). The period that begins after the three-year window has closed is referred to as the "B delay" or the "B period". ("C delays," delays resulting from interferences, secrecy orders, and appeals, are similarly treated but were not involved in the patent applications underlying this suit.)

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[1] Certain reasons for exceeding the three-year pendency period are excluded, see 35 U.S.C. § 154(b)(1)(b)(i)-(iii), as are periods attributable to the applicant's own delay. See 35 U.S.C. § 154(b)(2)(C).

The extensions granted for A, B, and C delays are subject to the following limitation:

> **(A) In general.**--To the extent that periods of delay attributable to grounds specified in paragraph (1) overlap, the period of any adjustment granted under this subsection shall not exceed the actual number of days the issuance of the patent was delayed.

35 U.S.C. § 154(b)(2)(A). This provision is manifestly intended to prevent double-counting of periods of delay, but understanding that intent does not answer the question of what is double-counting and what is not. Proper interpretation of this proscription against windfall extensions requires an assessment of what it means for "periods of delay" to "overlap."

The PTO, pursuant to its power under 35 U.S.C. § 154(b)(3)(A) to "prescribe regulations establishing procedures for the application for and determination of patent term adjustments," has issued final rules and an "explanation" of the rules, setting forth its authoritative construction of the double-counting provision. The rules that the PTO has promulgated essentially parrot the statutory text, see 37 C.F.R. § 1.703(f), and so the real interpretive act is found in something the PTO calls its Explanation of 37 CFR 1.703(f) and of the United States Patent and Trademark Office Interpretation of 35 U.S.C. § 154(b)(2)(A), which was published on June 21, 2004, at 69 Fed. Reg. 34238. Here, the PTO "explained" that:

> the Office has consistently taken the position that if an application is entitled to an adjustment under the three-year pendency provision of 35 U.S.C. § 154(b)(1)(B), the entire period during which the application was pending before the Office (except for periods excluded under 35 U.S.C. § 154(b)(1)(B)(i)-(iii)), and not just the period beginning three years after the actual filing date of the application, is the relevant period under 35 U.S.C. § 154(b)(1)(B) in determining whether periods of delay "overlap" under 35 U.S.C. 154(b)(2)(A).

69 Fed. Reg. 34238 (2004) (emphasis added). In short, the PTO's view is that any administrative delay under § 154(b)(1)(A) overlaps any 3-year maximum pendency delay under § 154(b)(1)(B): the applicant gets credit for "A delay" or for "B delay," whichever is larger, but never A + B.

In the plaintiffs' submission, this interpretation does not square with the language of the statute. They argue that the "A period" and "B period" overlap only if they occur on the same calendar day or days. Consider this example, proffered by plaintiff: A patent application is filed on 1/1/02. The patent issues on 1/1/08, six years later. In that six-year period are two "A periods," each one year long: (1) the 14-month deadline for first office action is 3/1/03, but the first office action does not occur until 3/1/04, one year late; (2) the 4-month deadline for patent issuance after payment of the issuance fee is

1/1/07, but the patent does not issue until 1/1/08, another year of delay attributable to the PTO. According to plaintiff, the "B period" begins running on 1/1/05, three years after the patent application was filed, and ends three years later, with the issuance of the patent on 1/1/08. In this example, then, the first "A period" does not overlap the "B period," because it occurs in 2003-04, not in 2005-07. The second "A period," which covers 365 of the same days covered by the "B period," does overlap. Thus, in plaintiff's submission, this patent holder is entitled to four years of adjustment (one year of "A period" delay + three years of "B period" delay). But in the PTO's view, since "the entire period during which the application was pending before the office" is considered to be "B period" for purposes of identifying "overlap," the patent holder gets only three years of adjustment.

Chevron Deference

We must first decide whether the PTO's interpretation is entitled to deference under Chevron v. NRDC, 467 U.S. 837 (1984). No, the plaintiffs argue, because, under the Supreme Court's holdings in Gonzales v. Oregon, 546 U.S. 243 (2006), and United States v. Mead Corp., 533 U.S. 218 (2001), Congress has not "delegated authority to the agency generally to make rules carrying the force of law," and in any case the interpretation at issue here was not promulgated pursuant to any such authority.

See Gonzales, 546 U.S. at 255-56, citing Mead, 533 U.S. at 226-27. Since at least 1996, the Federal Circuit has held that the PTO is not afforded Chevron deference because it does not have the authority to issue substantive rules, only procedural regulations regarding the conduct of proceedings before the agency. See Merck & Co. v. Kessler, 80 F.3d 1543, 1549-50 (Fed. Cir. 1996).

Here, as in Merck, the authority of the PTO is limited to prescribing "regulations establishing procedures for the application for and determination of patent term adjustments under this subsection." 35 U.S.C. § 154(b)(3)(A) (emphasis added). Indeed, a comparison of this rulemaking authority with the authority conferred for a different purpose in the immediately preceding section of the statute makes it clear that the PTO's authority to interpret the overlap provision is quite limited. In 35 U.S.C. § 154(b)(2)(C)(iii) the PTO is given the power to "prescribe regulations establishing the circumstances that constitute a failure of an applicant to engage in reasonable efforts to conclude processing or examination of an application" (emphasis added) -- that is, the power to elaborate on the meaning of a particular statutory term. No such power is granted under § 154(b)(3)(A). Chevron deference does not apply to the interpretation at issue here.

Statutory Construction

Chevron would not save the PTO's interpretation, however, because it cannot be reconciled with the plain text of the statute. If the statutory text is not ambiguous enough to permit the construction that the agency urges, that construction fails at Chevron's "step one," without regard to whether it is a reasonable attempt to reach a result that Congress might have intended. See, e.g., MCI v. AT&T, 512 U.S. 218, 229 (1994) ("[A]n agency's interpretation of a statute is not entitled to deference when it goes beyond the meaning that the statute can bear.").

The operative question under 35 U.S.C. § 154(b)(2)(A) is whether "periods of delay attributable to grounds specified in paragraph (1) overlap." The only way that periods of time can "overlap" is if they occur on the same day. If an "A delay" occurs on one calendar day and a "B delay" occurs on another, they do not overlap, and § 154(b)(2)(A) does not limit the extension to one day. Recognizing this, the PTO defends its interpretation as essentially running the "period of delay" under subsection (B) from the filing date of the patent application, such that a period of "B delay" always overlaps with any periods of "A delay" for the purposes of applying § 154(b)(2)(A).

The problem with the PTO's construction is that it considers the application delayed under § 154(b)(1)(B) during the

period before it has been delayed. That construction cannot be squared with the language of § 154(b)(1)(B), which applies "if the issue of an original patent is delayed due to the failure of the United States Patent and Trademark Office to issue a patent within 3 years." (Emphasis added.) "B delay" begins when the PTO has failed to issue a patent within three years, not before.

The PTO's interpretation appears to be driven by Congress's admonition that any term extension "not exceed the actual number of days the issuance of the patent was delayed," and by the PTO's view that "A delays" during the first three years of an applications' pendency inevitably lead to "B delays" in later years. Thus, as the PTO sees it, if plaintiffs' construction is adopted, one cause of delay will be counted twice: once because the PTO has failed to meet and administrative deadline, and again because that failure has pushed back the entire processing of the application into the "B period." Indeed, in the example set forth above, plaintiffs' calendar-day construction does result in a total effective patent term of 18 years under the (B) guarantee, so that - again from the PTO's viewpoint -- the applicant is not "compensated" for the PTO's administrative delay, he is benefitted by it.

But if subsection (B) had been intended to guarantee a 17-year patent term and no more, it could easily have been written that way. It is true that the legislative context -- as

distinct from the legislative history -- suggests that Congress may have intended to use subsection (B) to guarantee the 17-year term provided before GATT. But it chose to write a "[g]uarantee of no more than 3-year application pendency," 35 U.S.C. § 154(b)(1)(B), not merely a guarantee of 17 effective years of patent term, and do so using language separating that guarantee from a different promise of prompt administration in subsection (A). The PTO's efforts to prevent windfall extensions may be reasonable -- they may even be consistent with Congress's intent -- but its interpretation must square with Congress's words. If the outcome commanded by that text is an unintended result, the problem is for Congress to remedy, not the agency.

JAMES ROBERTSON
United States District Judge

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLUMBIA

WYETH, *et al.*,

Plaintiffs,

v.

JON W. DUDAS, Under Secretary of Commerce for Intellectual Property and Director of U.S. Patent and Trademark Office,

Defendant.

Civil Action No. 07-1492 (JR)

ORDER

For the reasons stated in the accompanying memorandum opinion, plaintiffs' motion for summary judgment [12] is **GRANTED** and defendant's motion for summary judgment [16] is **DENIED**. The case is remanded to the agency for further proceedings that are consistent with this opinion.

JAMES ROBERTSON
United States District Judge